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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,913	11/29/2004	Weikert Hendrikus Van Gilst	2578-6485US	7130

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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,913	VAN GILST, WEIKERT HENDRIKUS	
	Examiner	Art Unit	
	Robert B. Mondesi	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-23* is/are pending in the application.

4a) Of the above claim(s) *6-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 5 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the amendment filed October 27, 2006.

Status of the Claims

Claims 3-4 have been canceled. **Claim 23** has been added. **Claims 6-22** have been withdrawn for pertaining to non-elected inventions. **Claims 1-2, 5 and 23** are currently pending and under examination.

Withdrawal of Objections and Rejections

The objections and rejections not explicitly restated below are withdrawn due to applicants' response in amendment filed October 27, 2006.

Claim Rejections - 35 USC § 112

The rejection of **claims 1-5** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn due to applicants' amendment to the claims provided in amendment filed October 27, 2006.

The rejection of **claims 1-5** under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment, does not reasonably provide enablement for prevention is withdrawn due to applicants' amendment to the claims provided in amendment filed October 27, 2006.

The rejection of **claims 1-5** under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn due to applicants' amendment to the claims provided in amendment filed October 27, 2006.

Maintenance of rejections

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-2 and 5 remain rejected and **claim 23** is rejected under 35 U.S.C. 103(a) as being unpatentable over Brines et al., US Patent No. 6,531,121 in view of Berg et al. US Patent No. 5, 506,118.

Brines et al. teach a method of treating a patient suffering form chronic coronary syndrome, wherein the coronary syndrome is cardiac failure or chronic ischemia and the patient is non-anemic comprising administering a medicament comprising erythropoietin, wherein the erythropoietin is recombinantly produced (column 1, lines 65-68 through column 2, lines 1-3; column 3, line 26-27; column 4, lines 13-25, column 10, lines 37, column 18, lines 7-12, Example 3, column 19, lines 23-36).

Brines et al. do not teach that the said erythropoietin was produced in a host cell expressing at least the E1A protein of adenovirus.

Berg et al. teach that the E1A gene product is used in cells to enhance expression activity (Abstract and column 4, lines 7-13).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the EA1 protein for the advantages of increasing cellular protein expression as taught by Brines et al. and Berg et al., see Berg et al. at column 4 lines 7-13.

Note to applicants, the rejection above applies to the newly added claim 23, because as it appears, **claim 23** does not contain any new limitations and is essentially a re-write of **claim 1**.

Response to applicants' arguments

In regards to the rejection of **claims 1-2 and 5** under 35 U.S.C. 103(a) as being unpatentable over Brines et al. in view of Berg et al., applicants assert that the claims as amended refer to chronic heart failure and Brines does not relate to chronic heart failure (the term "chronic heart failure" is not found in Brines).

Applicants' arguments have been considered but have not been found persuasive. A close look at the applicants application, including a search for the term "chronic heart failure" did not reveal any evidence that the applicants' have defined the said term in any other manner besides the acceptable definition found in the art (in fact the exact term "chronic heart failure" was not cited anywhere in the specification of the instant application, which has coincidently led to a new matter rejection, see below).

The status of the art relevant to the instant invention teaches that many definitions of chronic heart failure exist, but only selective features of this complex syndrome are highlighted. None is entirely satisfactory. A simple objective definition of CHF is currently impossible as there is no cut off value of cardiac dysfunction or change in flow, pressure, dimension, or volume that can be used reliably to identify patients with heart failure. The diagnosis of heart failure relies in clinical judgment based on a history, physical examination, and appropriate investigations. For practical purposes, the essential components of heart failure have been found to be a syndrome in which the

patients should have the following features: symptoms of **heart failure**, typically breathlessness or fatigue, either at rest or during exertion and **objective evidence of cardiac dysfunction at rest** (Swedberg et al., page 4, column 2, lines 11-25).

Brines et al. may not specifically have stated that their invention is a method of treatment of "chronic heart failure" but, however; Brines et al. have clearly indicated that the method of their inventions involves alleviating symptoms that are associated with the commonly understood definition of chronic hear failure, see Berg et al. column 17, lines 29-43 via the administering of EPO.

Furthermore in response to applicant's arguments, the recitation chronic heart failure has only been given limited patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

New Objection(s) and Rejection(s)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 5 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have amended **claim 1** to specifically include the term "chronic heart failure" and have indicated support for the said term exists on page 2, lines 26-31; however a search of the specification of the instant application does not indicate in single instance were the term "chronic heart failure" has been used, defined or cited.

Therefore the question is raised as to whether applicants' amendment to claim has raised new issues with regards to new matter. The failure to meet the written description requirement of 35 U.S.C. 112, first paragraph, commonly arises when the claims are changed after filing to either broaden or narrow the breadth of the claim limitations, or to alter a numerical range limitation or to use claim language which is not synonymous with the terminology used in the original disclosure. To comply with the written description requirement of 35 U.S.C. 112, para. 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or 365(c), each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of the cell line containing EPO that is recombinantly produced in an immortalized human cell line PER.C6 deposited under European Collection of Animal Cell Cultures ECACC no. 96922940. It is not clear that cDNA encoding recombinant EPO deposited as ECACC no. 96922940 is known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Applicant's referral to the deposit of the recombinantly produced EPO on page 5, pargraph 0017, lines 8-9 of the specification is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made

under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same

as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice

Claims 1-2, 5 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* expression of EPO as in **isolated** host cell, does not reasonably provide enablement for *in vivo* expression of EPO, as in host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in

determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the relative skill of those in the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low

likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1-2 .Breadth of the claims and the nature of the invention..

In regards to the method of the invention and the breadth of the claims the broadest interpretation that applies is a method of treating a patient suffering form chronic heart failure, the method comprising producing erythropoietin (EPO) in a host cell expressing (*in vitro* and *in vivo*) at least the Early Region 1A (E1A) for the treatment of a patient suffering from a chronic heart failure; and administering said medicament to said patient.

3-4. The state of prior art and the level of predictability in the art.

The prior art is silent with regards to the in vivo use of the method of the invention with regards to expressing EPO in a host such as gene therapy and therefore the level of predictability is low.

However in regards to the in vitro expression of EPO in an **isolated** host cell Brines et al. teach a method of treating a patient comprising administering a medicament comprising erythropoietin, wherein the erythropoietin is recombinantly produced.

5. The relative skill in the art.

The relative skill in the art as it relates to the method of the invention is characterized by that of a M.D. or Ph. D. level individual.

6-7. The amount of guidance present and the existence of working examples.

The amount of guidance present in the specification of the present application in regards to the *in vivo* expression of EPO, as in gene therapy, is extremely low.

Applicants have not provided any examples in the present application indicating the *in vivo* expression of EPO, as in gene therapy.

Applicants have provided same guidance but no examples in regards to the *in vitro* expression of EPO in an **isolated** host cell, see page 7, paragraph 0022.

8. The quantity of experimentation necessary.

The amount of experimentation that is required is undue: while the in vitro expression of EPO in an **isolated** host cell is routine, the *in vivo* expression of EPO in instances that lead to a method of gene therapy is not routine and requires more experimentation. Therefore, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

It must be noted that the issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The Applicants make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "... scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance,

determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQZd at 1404 (Fed. Cir. 1988). Therefore, for the instant specification to be enabling, it needs to provide direction/guidance regarding gene therapy using EPO expression in a human cell. Absent sufficient guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and insufficient working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting express EPO in a human cell or other non-isolated host cells encompassed by the claimed invention would constitute undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-2, 5 and 23 are rejected under 35 U.S.C. 101 because as written, **claims 1-2, 5 and 23,** do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences

between the claimed products and the naturally occurring products. In the absence of the hand of man, he naturally occurring products are considered nonstatutory subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U. S. 566 (1974); *American Fruit Growers v. Brogdex Co.*, 283 U. S. 1 (1931); *Funk Brothers Seed Co. v. Kalo Inoculant*, 33 U. S. 127 (1948); and *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or purified". See MPEP 2105.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B. Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert B Mondesi
Examiner
Art Unit 1652

Robert B. Mondesi
1-31-2007